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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/773,394	01/31/2001	Lars Wiklund	P/2432-37	5538

7590

08/07/2003

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EXAMINER

BAHAR, MOJDEH

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 08/07/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/773,394

Applicant(s)

WIKLUND ET AL.

Examiner

Mojdeh Bahar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Applicant's response to the first office action and amendment submitted February 28, 2003 is acknowledged. Applicant's amendment has overcome the claim objections in the previous office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Note that the newly added negative limitations the first composition "being devoid of ammonium" and the second composition "being devoid of alpha-ketoglutarate and alpha-ketoglutaric acid" does not have support in the specification. The specification does not require that the first composition be devoid of ammonium, nor does it require that the second composition be devoid of alpha-ketoglutarate and alpha-ketoglutaric acid.

In his remarks, applicant has referred to page 10 of the specification, note that no support for the negative provide herein can be found on this page.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

Claims 1-2, 4-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Veech (USPN 5,719,119) and Vinnars (USPN 5,310,768).

Veech (USPN 5,719,119) teaches a parenteral nutrition solution comprising alpha-ketoglutarate and ammonium, see Table 9, col.20, examples 1.4-1.5. Veech also teaches the employment of the parenteral nutrition solution in a method of normalizing muscle and organ function, see claim 5 for example. Veech further teaches that post-traumatic or post-operative patients suffer from a negative nitrogen balance, col.7, line 55 to column 8 line 7. Veech also teaches alpha ketoglutarate and ammonium in an amino acid solution containing glutamate which can control the redox state of the mitochondria and therefore be useful in nitrogen-containing pharmaceutical compositions, see col. 13 line 5 to col. 14 line 20.

Vinnars (USPN 5,310,768) teaches a method of treatment of post operative and posttraumatic patients for improving glutamine content in skeletal muscle and preventing the reduction of protein synthesis capacity, hence also, improve the nitrogen balance and even make it positive by administering alpha-ketoglutarate, alone or in combination with other actives, see

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col. 2, lines 54-63 and abstract in particular. Vinnars teaches that the amount of alpha-ketoglutarate is at least 0.1g/kg body weight/day (which amounts to 312.5 micromoles/kg body weight per day), see col. 3, lines 6-12.

Veech and Vinnars do not particularly teach the dosing regimen herein in terms of micromoles per kilogram per minute, nor do they teach the administration of two separate compositions. Neither does it particularly teach the employment of a particular salt of ammonium.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a composition consisting essentially of alpha-ketoglutarate and an ammonium salt in the doses herein in a method of preserving bodily protein in catabolic patients.

One of ordinary skill in the art would have been motivated to employ ~~a~~ two separate compositions each consisting essentially of alpha-ketoglutarate or an ammonium salt in the doses herein in a method of preserving bodily protein in catabolic patients because both alpha-ketoglutarate and ammonium are known to be useful in methods of treating post-operative/post-traumatic patients and normalizing/preserving skeletal muscle glutamine/nitrogen content. Combining two agents which are known to be useful to improve nitrogen balance and preserve skeletal muscle individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. The employment of salts of known actives is within the skill of the Skilled Artisan and is therefore obvious. Optimization of amounts or variations in regimens, i.e., a single composition or two compositions comprising the same actives is within the skill of the artisan and is therefore obvious, absent evidence to the contrary.

Response to Arguments

Applicant's arguments have been considered but are not persuasive to remove the obviousness rejection. Applicant first argues that the claims as amended are drawn to two separate compositions, each containing only one of the actives herein, i.e., ammonium or alpha-ketoglutaric acid. Applicant further argues that Veech does not teach two separate compositions. Note that the rejection herein is an obviousness rejection, and not an anticipation rejection. As discussed in the body of the rejection, Veech teaches that the parenteral administration of a composition comprising both ammonium and alpha-ketoglutarate is known to be useful in post-traumatic patients. Optimization of amounts or variations in regimens, i.e., a single composition or two compositions comprising the same actives is within the skill of the artisan and is therefore obvious, absent evidence to the contrary. Note that the ultimate result of both the prior art and the instant claims is indistinguishable. Both methods supply the post-traumatic patient with ammonium and alpha-keto-glutarate concomitantly. Note that the variation of regimen is within the purview of the skilled artisan and is therefore obvious. Applicants aver unexpected benefits residing in the claimed subject matter, yet fail to ~~fail~~ set forth evidence substantiating this belief. Evidence as to unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). Note that attorney's arguments do not constitute a showing of unexpected results.

Applicant then states that the Vinnar patent does not teach the employment of ammonium in its composition and method. Note that Vinnar is a secondary reference employed to supplement the teachings of Veech. Moreover, Vinnar teaches that a composition comprising

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ketoglutarate and no ammonium can be employed in a parenteral nutrition program in post-traumatic patients. Therefore the skilled artisan in possession of the teachings of the prior art references herein can conclude that alpha ketoglutarate alone as well as in combination with ammonium is known to be useful in treating post-traumatic patients since Vinnars teaches a combination with alpha ketoglutarate and Veech teaches a composition comprising both alpha ketoglutarate and ammonium.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

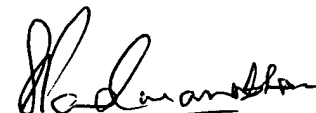
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
August 5, 2003



SREENI PADMANABHAN
PRIMARY EXAMINER

8/6/03